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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/338,221	06/22/99	PINES	E 22553/17

EXAMINER	
GUPTA, A	
ART UNIT	PAPER NUMBER
1653	8

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DATE MAILED: 10/11/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/338,221	PINES ET AL.	
	Examin r	Art Unit	
	Anish Gupta	1653	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-14 and 18-34* is/are pending in the application.

4a) Of the above claim(s) *18-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-14, in Paper No. 9 is acknowledged. Claims 18-34 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected Group II and Group III.

2. Applicant's election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that "it is believed that the claims are sufficiently related to be properly presented in a single application." This is not found persuasive because of the following reasons: Applicants subjective beliefs are not sufficient to traverse the restriction requirement. Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement and therefore the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-14 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

In claim recite that the composition comprises "fibrinogen from a sample of non-human, mammalian blood plasma with polyethylene glycol such that at least about 90% of the fibrinogen present in said sample is recovered..." However it is unclear what the composition comprise. That is, does the composition comprise only fibrinogen, which is recovered by subjecting non mammalian blood to PEG or does the composition comprise fibrinogen and PEG. Since it is unclear what the composition comprises, the claim is rendered indefinite.

The term "high yield" in the claims is a relative term which renders the claim indefinite. The term "high yield" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. A broad range or limitation

together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims recites the broad recitation of 25 mg/ml, and the claim also recites 10mg/ml or less which is the narrower statement of the range/limitation.

Claims have been amended to recite "said fibrinogen being made present at the site of treatment at a concentration of about 10mg/ml or less." However it is unclear if the fibrinogen is being made at the site of treatment or it is being made prior to the administration. The claim is unclear since it state "fibrinogen being made present at the site of treatment." Clarification is requested.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwarz et al. in view of Tripodi.

The claims are drawn to a therapeutic composition comprising fibrinogen.

Schwarz et al. teach a tissue adhesive composition for wound closures that comprises fibrinogen that is capable of cross-linking with fibrin-γ-chains after 3 to 5 minutes of incubation (see claim 1). The amount of fibrin in the composition is 90.6 mg/ml and 6.6 g of sodium citrate (see col. 3-4, examples). The reference also teaches a composition that comprises aminocaproic acid (see table 1). The reference further states that the plasma proteins can be obtained from animal origins (see col. 1. 57-60). The difference between the prior art and the instant application is that the reference does not specifically teach the animal origin of fibrinogen and does not teach the concentrations claimed.

However, the reference of Tripodi teach a fibrinogen based composition that is derived from bovine plasma (see abstract). The reference states that there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen (see page 5, lines 29-30). The fibrinogen composition disclosed is used as a adhesive for means of wound closing (see page 10, lines 23-25). Therefore, since the compositions of both Schwarz et al. and Tripodi are used for wound closures and since there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen, it would have been obvious to use bovine plasminogen for a tissue adhesive composition for wound closures.

As for the concentrations claimed, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Abler*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955)

6. Claims 1-3, 7-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stroetmann et al. ('650) or Stroetmann et al. ('655) in view of Tripodi et al.

The claims are drawn to a therapeutic composition comprising fibrinogen.

The references of Stroetmann et al. teach a plasma derivative for supporting wound closure and healing that contains fibrinogen and thrombin (see claims and see col. 12, lines 6-44 in '655). The plasma derivative is rapidly soluble in body fluids and therefore may be immediately and directly applied for wound closure. Due to the admixture of thrombin, rapid polymerization occurs after partial passing into solution and or dissolution and a viscous, well adhering would closing material is formed (see col. 2, lines 63-68 and col. 3, lines 1-3 in '650 and see col. 9 and 10 in '655). The references disclose that the fibrinogen used can be lyophilized (see example 1 in both). The difference between the prior art and the instant application is that the reference does not teach the exact concentration claimed and does not teach the teach the animal origin of fibrinogen, such as bovine fibrinogen, and pH of the solution.

However, the reference of Tripodi teach a fibrinogen based composition that is derived from bovine plasma (see abstract). The reference states that there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen (see page 5, lines 29-30). The fibrinogen composition disclosed is used as a adhesive for means of wound closing (see page 10, lines 23-25). Therefore, since the compositions of both reference of Stroetmann et al. and Tripodi are used for wound closures, it would have been obvious to substitute bovine plasminogen for human plasminogen in a tissue adhesive composition for wound closures because there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen.

Further, since the plasma derivative is used for wound closure, it would have been obvious to one of ordinary skill in the art to have a pH for the solution within a physiological pH range, which is routinely between pH 7-8. As for the concentration, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Abler*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

7. Claims 1-3, 5, 7-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stroetmann et al. ('650) or Stroetmann et al. ('655) in view of Tripodi et al. in further view of Farrell et al.

The claims are drawn to a therapeutic composition comprising fibrinogen.

The references of Stroetmann et al. in view of Tripodi have been discussed supra. The difference between the prior art and the instant application is that the reference does not teach the use of ϵ-amino-caproic acid.

However, Farrell et al. teach that for compositions containing Thrombin and Fibrinogen, the use ϵ-amino-caproic acid is effective in inhibiting fibrinogenolysis (see abstract). Therefore, it would have been obvious to one of ordinary skill in the art to use ϵ-amino-caproic acid in the plasma derivative to inhibit fibrinogenolysis.

8. Claims 1-11 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stroetmann et al. ('650) or Stroetmann et al. ('655) in view of Tripodi et al., Farrell et al. and Miyano et al.

The claims are drawn to a therapeutic composition comprising fibrinogen.

The references of Stroetmann et al. in view of Tripode and Farrell et al. have been discussed supra. The difference between the prior art and the instant application is that the reference does not teach the use of sodium citrate.

However, Miyano et al. teach that sodium citrate may be further added as auxiliary stabilizers to the aqueous solution of fibrinogen. These additives are generally used in a concentration of 0.001 to 1M in the fibrinogen solution (col. 2, lines 49-55). Therefore, it would have been obvious to one of ordinary skill in the art to use sodium citrate in the plasma derivative of Stroetmann et al. to stabilize the solution.

9. Claims 2 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stroetmann et al. ('655) in view of Richter (abstract) and Tripode et al.

The claims are drawn to a therapeutic composition comprising fibrinogen.

Stroetmann et al. teach a fibrinogen containing lyophilized composition, for treating wounds, comprising fibrinogen and further comprising glycoproteins such as albumin, fibronectin and globulin (see claims 1 and 8). The addition of these glycoproteins provides flexibility, mechanical strength and stability to the dry composition to prevent a loss of activity of the coagulation enzymes during long periods of storage (see col 4, lines 65-69 and col. 5, lines 1-7). The glycoproteins are incorporated as 5 to 25% of the weight of the final preparation (see col. 5, lines 3). The difference between the prior art and the instant application is that the reference does not teach the presence of plasminogen and bovine fibrinogen.

In Stroetmann et al., the method of isolating the fibrinogen involves precipitation with ethanol, the subsequent isolation and again precipitated by adding glycine. As indicated by Richter et al., this method results in the presence of .01% or less plasminogen. Therefore, since the method isolating the fibrinogen, in Stroetmann et al, from plasma results in the presence of plasminogen, at a level of less than 1%, the composition of Stroetmann et al. would contain plasminogen.

Further, the reference of Tripodi teach a fibrinogen based composition that is derived from bovine plasma (see abstract). The reference states that there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen (see page 5, lines 29-30). The fibrinogen composition disclosed is used as a adhesive for means of wound closing (see page 10, lines 23-25). Therefore, since the compositions of both reference of Stroetmann et al. and Tripodi are used for wound closures, it would have been obvious to substitute bovine plasminogen for human plasminogen in a tissue adhesive composition for wound closures because there is only a small degrees of disparity between human fibrinogen and bovine fibrinogen. As for the concentration claimed, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."_*In re Abler* , 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can normally be reached on (703)308-2923. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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